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10/086,748

02/28/2002

Paul K. Wolber

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AGILENT TECHNOLOGIES INC.
INTELLECTUAL PROPERTY ADMINISTRATION,LEGAL DEPT.
MS BLDG. E P.O. BOX 7599
LOVELAND, CO 80537

EXAMINER

ZHOU, SHUBO

ART UNIT

PAPER NUMBER

1631

NOTIFICATION DATE

DELIVERY MODE

01/28/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com

Office Action Summary	Application No. 10/086,748	Applicant(s) WOLBER ET AL.	
	Examiner SHUBO (Joe) ZHOU	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 10-12, 15, 18 and 20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10-12, 15, 18, and 20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment filed 11/5/08 is acknowledged and entered.

Claims 1-8, 10-12, 15, 18, and 20 are currently pending and under consideration.

Claim Rejections-35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10-12, 15, 18, and 20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are amended to recite "a set of calibrating features, each containing calibrating probes that indiscriminately hybridize, under stringent conditions, to specific target molecules in sample solutions...." Applicant did not provide, and the Office were unable to find support for the new limitation with regard to the manner of the hybridization, i.e. indiscriminately to specific target molecules. The specification does not provide adequate description for the limitation and is thus new matter.

This rejection is reiterated from the previous Office action. Applicant argues on 11/5/08 that the specification on page 35 support the new limitation. This is not found persuasive because the pointed paragraph is referring to antibody binding to antigens.

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The instant claims however refer to calibration probes that indiscriminately hybridize, under stringent conditions, to specific target molecules in sample solutions. This is not persuasive because when the terms “hybridize” and “stringent conditions” are used, one skilled in the art would understand that this refers to nucleic acid hybridizing to nucleic acids, not antibody binding to antigen.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The rejection of claims 1-8, 10-12, 15, 18, and 20 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention set forth in the previous Office action is hereby withdrawn in view of applicant’s argument on page 7 of the response filed 11/5/08, which is considered persuasive.

Claim Rejections-35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7-8, and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Lockhart et al. (IDS document: WO 97/10365, 3/20/1997).

The claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that hybridize indiscriminately to specific target molecules in a sample to produce a signal intensity, and normalizing signals of features on the array using the calibrating probes by calculating a collective calibrating signal intensity. Due to lack of a specific definition for the term “collective calibrating signal intensity” in the specification, it is interpreted as total signal intensities of the calibrating probes (collective: assembled or accumulated into a whole.

Dictionary.com <http://dictionary.reference.com/search?q=collective>).

Lockhart et al. disclose a method of using oligonucleotide array for monitoring gene expression. The method comprises using an array containing not only oligonucleotide probes referred to as “test probes”, but also control probes used for calibration. The control probes include normalization controls, expression level controls such as probes from housekeeping genes, and mismatch controls. In one embodiment, Lockhart et al. teach that the difference between signal intensities of a perfect match (PM) probe and a mismatch (MM) probe for each pair of PM and MM are calculated, and then the average of the differences for all the pairs is calculated. See page 61, first paragraph and page 103, claims 66-67. It would be readily recognized by one of skill in the art that when the average difference is calculated, a total intensity of the difference between the PM and MM must have also been calculated. Consequently, the total intensities of all MM probes are also calculated. All the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes.

Lockhart et al. also disclose that for a mismatch control probe, one or more mismatches are selected such that under appropriate hybridization conditions (e.g. stringent conditions) the mismatch probe would not hybridize or would hybridize to a significantly lesser extent to target probes. See page 36. Accordingly, one skilled in the art would understand that this hybridization under high stringent condition would be nonspecific or indiscriminate hybridization.

As to the limitation that producing signal intensities upon reading of calibrating probes proportional to the total concentration of target molecules in the sample, it would be readily recognized by one of skill in the art that it is an inherent principle of using microarray for assessing gene expression that the signals produced by hybridization of probes on the array with the target molecules in the sample are indicative of the levels of target molecules in the sample, i.e. signal being proportional to the concentration of target molecules in the sample. As to the limitation “a set of features containing probes that hybridize to specific target molecules under stringent conditions,” the specific probes, i.e. the “test probes” on the array of Lockhart et al., are probes that would hybridize to specific target molecules in a sample under stringent conditions.

In regard to claims 7-8, which require that a set of similar calibrating signal intensities that each covers a discrete range of signal intensities generated from the features of the array, Lockhart et al. teach that each PM signal intensity is calibrated by calculating the difference between signal intensities of the PM and its corresponding MM. The signal intensity for every PM probe is similarly calibrated. The average difference for all PM/MM is also calculated. Each signal can then be calibrated thereupon. Each of these PM-MM signal intensities is interpreted as a calibrating signal

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intensity. Since all the differences of PM-MM are calculated similarly, they are interpreted as similar calibrating signal intensities. Because these differences of PM-MM as a whole represent the signal intensities for all the probes on the array, they cover the entire span, i.e. overall range of signal intensities generated from the array.

Applicant's arguments filed 11/5/08 have been fully considered but they are not persuasive. Applicant argues about the paragraph pointed to by the examiner as support on page 61 of Lockhart et al. but do not point out why the paragraph does not support that the difference between signal intensities of a perfect match (PM) probe and a mismatch (MM) probe for each pair of PM and MM, even if a subset, are calculated, and then the average of the differences for all the pairs, of the subset, is calculated. It would be readily recognized by one of skill in the art that when the average difference of the subset is calculated, a total intensity of the difference between the PM and MM of the subset must have also been calculated. Consequently, the total intensities of all MM probes of the subset are also calculated. See page 8. With regard to the examiner's interpretation that "[a]ll the control probes disclosed by Lockhart et al. are interpreted as calibrating probes as in the instant claims because they are used to calibrate the signals of the test probes," applicant argues that the term calibration features should have only one scope and it is the calibrating features that hybridize to a majority of target molecules in sample solutions. See page 9. This is not found persuasive because applicant appears to be arguing limitation that is not recited in the claims. The claims do not require that the calibrating features hybridize to the majority of target molecules.

Claim Rejections-35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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11. Claims 2-3, 5, and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, 7-8 and 15 above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Lewin, B., (Genes IV, 1990, Oxford University Press).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization, as is in claims 2-3 and 5, or hybridize to a majority of target molecules in the sample solution, as is in claims 10-12, and normalizing signals of features on the array using the calibrating probes by calculating a collective signal intensity. Claims 2-3 recite that the calibrating probes are poly(A) oligonucleotides, and claim 5 recites that the calibrating probes are oligonucleotides complementary to a synthetic nucleotide sequence appended to primers for reverse transcription of the mRNA molecules.

Lockhart et al. is applied as with claims 1, 7-8 and 15.

Lockhart et al. do not explicitly teach (1) that poly(A) oligonucleotides are used as calibrating probes; (2) that the calibrating probes are oligonucleotides complementary to a synthetic nucleotide sequence appended to primers for reverse transcription of the mRNA molecules; and (3) that the calibrating probes hybridize to a majority of the target molecules in the sample solution to which the array is exposed.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the “probe spots”, the array also comprises “calibration spots” and “control spots” (column 4, lines

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12-20). Chenchik et al. indicate that the calibrating and control spots are to “provide other useful information, such as background or basal level of expression, and the like”, and such spots “serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array” (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using poly(A) oligonucleotides as calibrating spots, they do motivate/suggest doing such by emphasizing that the calibrating probes should not be unique to a particular target in the sample, but “common” to the targets (column 8, lines 50-67).

Lewin teaches that poly(A) tail is common to eukaryotic, such as human mRNA. See pages 178-179.

Since the target molecules contained in the sample solutions to which the array is exposed for hybridization in the method disclosed by Lockhart et al. are cDNAs, and since the cDNAs are derived from mRNAs by reverse transcription using oligo(dT) as primers followed by PCR amplification (Lockhart et al. page 39), it would have been obvious to one of ordinary skill in the art that oligo(dT) or poly(A) would be commonly present in the cDNA targets due to the way they are made, and one of ordinary skill in the art would have been motivated by Chenchik et al. to modify the method of Lockhart et al. to use calibrating probes that are common to the target molecules, and would have been motivated by Lewin to include poly(A) oligonucleotides on the array as extra calibrating probes. Such poly(A) oligonucleotides would hybridize to the majority of the target molecules because of the presence of oligo(dT) therein. Further, such poly(A) oligonucleotides calibrating probes would be complementary to the oligo(dT) portion of the target molecules, which oligo(dT) is a synthetic nucleotide sequence that is appended

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to primers for reverse transcription of the mRNA molecules during the process of preparing target molecules for hybridization. This thus reads on the specific requirement by claim 5.

There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al. provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making poly(A) oligonucleotides would have been known and routine skill in the art. Note that by poly(A) oligonucleotides it is meant that the oligonucleotides consist of, or comprise, consecutive multiple "As".

Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the examiner does not state what motivation would have been to search for probes that are common to the targets in the sample solution. See page 12. This is not found persuasive because it is clearly stated in the previous Office action that it is Chenchik's emphasizing that the calibrating probes should not be unique to a particular target in the sample, but "common" to all the targets (column 8, lines 50-67) that serves the motivation for searching probes that are common to the targets. Applicant further argues that Chenchik does not teach normalization procedures based on calibration probes, etc. See pages 12-13. This is not found persuasive. It is not disputed that Chenchick does not teach all the limitations of the claims. However, Chenchick does teach having calibration spots suggesting the importance of calibration. In this line of reasoning, again, Chenchick's suggestion that calibration probes should not be unique to a particular target but common to other targets. This suggestion would have motivated one having ordinary skill in the art to search for probes that are common to all targets. For cDNA targets, it would have been readily apparent to one having ordinary skill in the art

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that one of the features most common to most if not all cDNAs are the poly-T/A in the molecules as also taught by Lewin.

Applicant argues that the examiner withdrew the rejections in response to applicant's amendment filed 3/21/06, but did not respond to applicant's arguments in the response. It should be pointed out that in the Office action mailed 5/24/07, it was explicitly point out that the rejections were withdrawn "in view of the amendment to the claims filed 4/17/06." The amendment added the limitation that "each containing calibrating probes that hybridize to a majority of the target molecules." It is this new limitation that is not taught or suggested by the previously cited arts and the rejections were thus withdrawn. This limitation, however, was deleted in the amendment filed 8/17/07, which necessitated the reinstatement of the previously withdrawn rejections.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, 7-8, and 15 above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Darnell et al. (Molecular Cell Biology, Eds., 1990, published by Scientific American Books).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization or hybridize to a majority of target molecules in the sample solution, and normalizing signals of features on the array using the calibrating probes by

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calculating a collective signal intensity. Claim 4 also requires that the calibrating probes comprise Alu repeat sequences.

Lockhart et al. is applied as with claims 1, 7-8 and 15.

Lockhart et al. do not explicitly recite that oligonucleotide comprising Alu sequences are used as calibrating probes.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the “probe spots”, the array also comprises “calibration spots” and “control spots” (column 4, lines 12-20). Chenchik et al. indicate that the calibrating and control spots are to “provide other useful information, such as background or basal level of expression, and the like”, and such spots “serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array” (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using poly(A) oligonucleotides as calibrating spots, they do motivate/suggest doing such by emphasizing that the calibrating probes should not be unique to a particular target in the sample, but “common” to the targets (column 8, lines 50-67).

Darnell et al. teach that Alu sequence is common to human genes and mRNA (see pages 373-374).

A person of ordinary skill in the art would have been motivated by Chenchik et al. to include calibrating probes that are common to the targets in the sample solution to modify Lockhart et al. to provide more calibrating probes for the microarray analysis.

The teaching of Darnell et al. makes it obvious to one of ordinary skill in the art that such common Alu sequence would meet the requirement for a calibrating probe set by Chenchik et al. Thus, one of ordinary skill in the art would have been motivated by Chenchik et al. and Darnell et al. to modify the method of Lockhart et al. to include oligonucleotides comprising Alu sequences on the array as extra calibrating probes. There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al. provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making oligonucleotides comprising Alu sequence would have been known and routine skill in the art.

Applicant's arguments are the same as those for the above rejections with regard to Lockhart et al. and Chenchick, the arguments are not persuasive for the same reasons set forth above. Again, Chenchick only serves as a motivation to search for probes that are common to all targets to be used as calibrating probes.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lockhart et al. (WO 97/10365, 3/20/1997), as applied to claims 1, 7-8, and 15 above, in view of Chenchik et al. (US patent no. 6,077,673, Date of Patent: June 20, 2000) and further in view of Feinberg et al. (Analytical Biochemistry, Vol. 132, pages 6-13, 1983).

The instant claims are drawn to a method of calibrating molecular array data comprising using a molecular array containing calibrating probes that either hybridize to a sufficient fraction of target molecules in a sample solution to which the array is exposed for hybridization, and normalizing signals of features on the array using the calibrating

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probes by calculating a collective signal intensity. Claim 6 also requires that the calibrating probes are random sequence oligonucleotide.

Lockhart et al. is applied as with claims 1, 7-8 and 15.

Lockhart et al. do not explicitly recite that random sequence oligonucleotide are used as calibrating probes.

Chenchik et al. disclose a nucleic acid microarray and a process of using same for gene expression monitoring. The array is exposed to a sample solution containing cDNA molecules derived from the mRNA from a biological sample. In addition to the “probe spots”, the array also comprises “calibration spots” and “control spots” (column 4, lines 12-20). Chenchik et al. indicate that the calibrating and control spots are to “provide other useful information, such as background or basal level of expression, and the like”, and such spots “serve in the normalization of mRNA abundance and standardization of hybridization signal intensity in the sample assayed with the array” (column 8, lines 50-67 and column 9). While Chenchik et al. do not explicitly disclose using poly(A) oligonucleotides as calibrating spots, they do motivate/suggest doing such by emphasizing that the calibrating probes should not be unique to a particular target in the sample, but “common” to the targets (column 8, lines 50-67).

Feinberg et al. teach a method of labeling a DNA by using a mixture of random hexamer as primers and state that the oligonucleotides bind to any DNA in high frequency. see page 6, abstract and pages 7-11).

A person of ordinary skill in the art would have been motivated by Chenchik et al. to include calibrating probes that are common to the targets in the sample solution to modify Lockhart et al. to provide more calibrating probes for the microarray analysis.

The teaching of Feinberg et al. makes it obvious to one of ordinary skill in the art that the random hexamer oligonucleotides would be ideal for a calibrating probe because it would meet the “common” standard proposed by Chenchik et al. Thus, one of ordinary skill in the art would have been motivated by Chenchik et al. and Feinberg et al. to modify the method of Lockhart et al. to include random hexamer oligonucleotides on the array as extra calibrating probes. There would have been a reasonable expectation of success because Lockhart et al. and Chenchik et al. provide the details of procedures for making an array, preparing cDNA samples for hybridization, and making random hexamer oligonucleotides would have been known and routine skill in the art, and the random primers would have been actually commercially available.

Applicant's arguments are the same as those for the above rejections with regard to Lockhart et al. and Chenchik, the arguments are not persuasive for the same reasons set forth above. Again, Chenchik only serves as a motivation to search for probes that are common to all targets to be used as calibrating probes. Feinberg et al. provides that the random hexamers bind to any DNA in high frequency. Again this feature of random hexamers meets the “commonness” for calibrating probes suggested by Chenchik.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL.

Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to

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expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Shubo (Joe) Zhou/

SHUBO (JOE) ZHOU, PH.D.

PRIMARY EXAMINER

